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Safety and efficacy of a feed additive consisting of Sepiolitic clay for all animal species (Mineria y Tecnologia de Arcillas SA - MYTA)

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Abstract

Following a request from the European Commission, the Panel on Additives and Products or Substances used in Animal Feed (FEEDAP) was asked to deliver a scientific opinion on the re-evaluation of the authorisation of Sepiolitic clay as a feed additive for all animal species. The FEEDAP Panel considered that Sepiolitic clay is unlikely to be absorbed. Harmful amounts of residues of any chemical component in edible tissues/products, as a consequence of the use of Sepiolitic clay as a feed additive, are not expected. Sepiolitic clay is not genotoxic and does not induce any toxicity effects following oral administration and, therefore, it was considered safe for the consumers. Based on the data available, the FEEDAP Panel concluded that Sepiolitic clay is safe for dairy cows and weaned piglets at 20,000 mg/kg feed. These conclusions were extrapolated to other dairy ruminants, pigs for fattening and other growing *Suidae*. The additive is considered safe for chickens for fattening at 10,000 mg/kg feed and for salmonids at 17,600 mg/kg feed. Considering that it is not possible to establish a comparable margin of safety in the four major species, the Panel cannot conclude on the safety of Sepiolitic clay for other animal species/categories. Owing to the dusting potential of the additive and its crystalline silica content, handling the additive is considered a risk by inhalation for the users. It is not irritant or corrosive to skin or eyes. Due to the nickel content, it is considered a skin and respiratory sensitiser. The additive is considered safe for the environment. The FEEDAP Panel concluded that Sepiolitic clay is efficacious as binder and anticaking agent in feed for all animal species under the proposed conditions of use.

Keywords: Sepiolitic clay, binder, anticaking agent, all animal species, safety, efficacy

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1. Introduction

1.1. Background and Terms of Reference as provided by the requestor

Regulation (EC) No 1831/2003[1] establishes the rules governing the Community authorisation of additives for use in animal nutrition. In particular, Article 10(2) of that Regulation also specifies that for existing products within the meaning of Article 10(1), an application shall be submitted in accordance with Article 7, at the latest one year before the expiry date of the authorisation given pursuant to Directive 70/524/EEC for additives with a limited authorisation period, and within a maximum of seven years after the entry into force of this Regulation for additives authorised without a time limit or pursuant to Directive 82/471/EEC.

The European Commission received a request from MYTA S.A.[2] for re-evaluation of the authorisation of the product Sepiolitic clay, when used as a feed additive for all animal species (category: technological additives; functional group: binders, anticaking agents).

According to Article 7(1) of Regulation (EC) No 1831/2003, the Commission forwarded the application to the European Food Safety Authority (EFSA) as an application under Article 10(2) (re-evaluation of an authorised feed additive). EFSA received directly from the applicant the technical dossier in support of this application. The particulars and documents in support of the application were considered valid by EFSA as of 9 August 2019.

According to Article 8 of Regulation (EC) No 1831/2003, EFSA, after verifying the particulars and documents submitted by the applicant, shall undertake an assessment in order to determine whether the feed additive complies with the conditions laid down in Article 5. EFSA shall deliver an opinion on the safety for the target animals, consumer, user and the environment and on the efficacy of the product Sepiolitic clay, when used under the proposed conditions of use (see Section 3.1.5).

1.2. Additional information

Sepiolitic clay is authorised as binder, anti-caking agent and coagulant for all animal species with a maximum content of 20,000 mg/kg feed.[3]

EFSA has adopted two opinions, one on the safety and efficacy of sepiolite when used alone (EFSA FEEDAP Panel, 2022) and another when used in combination with bentonite in feed for all animal species (EFSA FEEDAP Panel, 2013).

2. Data and methodologies

2.1. Data

The present assessment is based on data submitted by the applicant in the form of a technical dossier[4] in support of the authorisation request for the use of Sepiolitic clay as a feed additive.

The FEEDAP Panel used the data provided by the applicant together with data from other sources, such as previous risk assessments by EFSA or other expert bodies, peer-reviewed scientific papers, other scientific reports and experts' knowledge, to deliver the present output.

EFSA has verified the European Union Reference Laboratory (EURL) report as it relates to the methods used for the control of the sepiolite in animal feed. The Executive Summary of the EURL report can be found in Annex A.[5]

2.2. Methodologies

The approach followed by the FEEDAP Panel to assess the safety and the efficacy of Sepiolitic clay is in line with the principles laid down in Regulation (EC) No 429/2008[6] and the relevant guidance documents: Guidance on the identity, characterisation and conditions of use of feed additives

[1] Regulation (EC) No 1831/2003 of the European Parliament and of the Council of 22 September 2003 on additives for use in animal nutrition. OJ L 268, 18.10.2003, p. 29.
[2] Myta S.A., Paseo Independencia, 21. 6ª, 50001 Zaragoza, Spain.
[3] Commission Regulation (EC) No 2439/1999 of 17 November 1999 on the conditions for the authorisation of additives belonging to the group 'binders, anti-caking agents and coagulants' in feedingstuffs. OJ L 297, 18.11.1999, p. 8.
[4] FEED dossier reference: FAD-2010-0229.
[5] The full report is available on the EU Science Hub: https://joint-research-centre.ec.europa.eu/publications/fad-2010-0229_en
[6] Commission Regulation (EC) No 429/2008 of 25 April 2008 on detailed rules for the implementation of Regulation (EC) No 1831/2003 of the European Parliament and of the Council as regards the preparation and the presentation of applications and the assessment and the authorisation of feed additives. OJ L 133, 22.5.2008, p. 1.

(EFSA FEEEDAP Panel, 2017a), Guidance on the assessment of the safety of feed additives for the target species (EFSA FEEDAP Panel, 2017b), Guidance on the assessment of the safety of feed additives for the consumer (EFSA FEEDAP Panel, 2017c), Guidance on the assessment of the efficacy of feed additives (EFSA FEEDAP Panel, 2018), Guidance on the assessment of the safety of feed additives for the environment (EFSA FEEDAP Panel, 2019) and Guidance on studies concerning the safety of use of the additive for users/workers (EFSA FEEDAP Panel, 2012).

3. Assessment

The additive under assessment is a mixture of clay and non-clay fractions (hereby referred to as Sepiolitic clay) containing a minimum of 40% of sepiolite (mineral) and 25% illite. The applicant is seeking the re-evaluation of the use as technological additives (functional groups: (g) binders and (i) anticaking agents) at a maximum concentration of 20,000 mg/kg in complete feed for all species.

3.1. Characterisation

3.1.1. Characterisation of the additive

The feed additive Sepiolitic clay is specified as hydrated magnesium silicate of sedimentary origin, containing at least 40% sepiolite (hydrous magnesium silicate) and 25% illite (potassium and iron aluminium silicate) and free of asbestos. The Chemical Abstracts Service (CAS) number of sepiolite is 63800-37-3, the EC number is 264-465-3. The CAS number of illite is 12173-60-3 and the EC number is 601-803-4.

Sepiolitic clay originates from Spanish sepiolite deposits. Its major component is sepiolite (minimum 40%) and it further contains illite (potassium and iron aluminium silicate, minimum 25%) and carbonates (dolomite, calcium and magnesium carbonate, up to 35%). Possible traces of calcite and kaolinite are also expected.

The applicant characterised three products that differ in their granulometry (based on the size of the sieve), namely: product 1, product 2 and product 3.[7] The applicant provided results of the mineralogical analysis performed [redacted] and elemental analysis [redacted] on five batches of the three products (Tables 1 and 2, respectively).[8,9] The sepiolite content was in all cases above 40% and illite at least 25%.

Table 1: Mineralogical composition of the Sepiolitic clay products [redacted], results reported as mean percentages (minimum–maximum)

Name of the product[(a)]	Sepiolite (%)	Illite (%)	Quartz (%)	Feldspars (%)	Dolomite (%)
Product 1	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Product 2	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Product 3	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]

(a): Five batches.

Table 2: Results reported as mean (minimum-maximum) of elemental analysis of the Sepiolitic clay products [redacted]

Name of the product[(a)]	SiO_2 (%)	Al_2O_3 (%)	Fe_2O_3 (%)	CaO (%)	MgO (%)	Na_2O (%)	K_2O (%)	TiO_2 (%)	MnO (%)	P_2O_5 (%)	BaO (%)	SrO (%)
Product 1	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Product 2	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]

[7] The three products characterised by the applicant differ in terms of granulometry: 15/30, 30/100 (size ranging 0.590–0.149 mm) and < 100 (size bellow 0.149 mm).
[8] Technical dossier/Section II/Supplementary information (November 2021)/Annex_I.
[9] Technical dossier/Section II/Supplementary information (November 2021)/Annex_II.

Name of the product[(a)]	SiO_2 (%)	Al_2O_3 (%)	Fe_2O_3 (%)	CaO (%)	MgO (%)	Na_2O (%)	K_2O (%)	TiO_2 (%)	MnO (%)	P_2O_5 (%)	BaO (%)	SrO (%)
Product 3	[redacted]											

(a): Five batches.

Content of fibre-shaped particles were also analysed using [redacted] and confirmed that Sepiolitic clay does not contain fibres with length of 5 μm or larger.[10]

The applicant also submitted data on the content of asbestos using X-Ray diffraction and scanning electron microscopy (SEM) in one batch of each final product and confirmed the absence of asbestos.[11]

The data submitted demonstrate compliance with the proposed specifications.

Cadmium, lead, mercury, arsenic, nickel, dioxins and dioxin-like polychlorinated biphenyls (PCBs) were analysed [redacted][12] All of the samples showed values [redacted] for cadmium [redacted] Lead content ranged from [redacted] The analysed values for arsenic ranged from [redacted], mercury ranged from [redacted] (average content of [redacted] in product 1 and [redacted] in products 2 and 3). The content of nickel ranged from [redacted]. Fluorine was also analysed in the same batches and measured on average to be [redacted].

In the batches tested, dioxins ranged between [redacted]. The sum of dioxins and dioxin-like polychlorinated biphenyls (PCBs) was also provided for the same batches and ranged between [redacted].

The levels of the above detected impurities do not raise a safety concern (except nickel).

Sepiolitic clay is a solid in powder form. The bulk density of the three products was reported to be in the range [redacted], the true density in the range [redacted] and the moisture in the range [redacted].[13] Water retention ranged between 100% and 130%.

No data on solubility in water was submitted; however, the applicant stated that the additive is not soluble in water or in organic solvents.

The dusting potential of the additive was measured in triplicate for each of the three products, [redacted] (Table 3)[14]

Table 3: Dusting potential of three batches of each product measured with [redacted] and results reported as mean (minimum–maximum)

Name of the product	[redacted]			[redacted]		
	Inhalable fraction (mg/m³)	Thoracic fraction (mg/m³)	Respirable fraction (mg/m³)	Inhalable fraction (mg/m³)	Thoracic fraction (mg/m³)	Respirable fraction (mg/m³)
Product 1	[redacted]					
Product 2						
Product 3						

[10] Technical dossier/Section II/Supplementary information (November 2021)/Annex_VI.
[11] Technical dossier/Section III/Annexes sect. III/ Annex_III.3 and Annex III.4.
[12] Technical dossier/ Supplementary information (November 2021)/Annex_IV.
[13] Technical dossier/ Supplementary information (November 2021)/Annex_V.1 and AnnexV.2.
[14] Technical dossier/ Supplementary information (November 2021)/Annex_V.1.

The particle size distribution was measured [redacted] in the same batches.[15] In product 1, [redacted]. In product 2, [redacted]. In product 3, [redacted].

3.1.2. Manufacturing process

The clay is obtained by mining sepiolite deposits in Spain. The mineral is extracted, transported and once in the factory undergoes a first crushing into pieces of 0–20 mm. After this, it is spread into drying beds and is air-dried, then undergoes a second grinding and drying process using a rotary dryer with hot gasses. The dry product is passed through a griddle system separating the different granulometries.

3.1.3. Stability and homogeneity

Studies demonstrating shelf-life are not required for mineral-based products. No data on stability and homogeneity have been sent by the applicant.

3.1.4. Physico-chemical incompatibilities or interactions

The applicant has submitted a study to demonstrate that Sepiolitic clay has no masking effect on mycotoxins.[16] [redacted] No differences were observed in the mycotoxins levels between the positive control and the samples containing mycotoxins and the additive at 2%, indicating that Sepiolitic clay does not interfere with the analytical detection of mycotoxins in feeds.

The applicant submitted a study to demonstrate that inclusion of Sepiolitic clay [redacted] did not affect the analytical determination of enzyme activity [redacted], antimicrobial substances [redacted] or some diet components [redacted] in feeds. [redacted][17] The results of this study confirmed that the inclusion of the additive to a wide variety of feeds did not affect the analysis of such compounds. Contradictory results were obtained on the detection of a liposoluble vitamin (i.e. vitamin A) from analysis of different samples of feeds for pigs, which may suggest an issue with homogeneity of the vitamin in that feed.

3.1.5. Conditions of use

Sepiolitic clay is intended to be used as binder and anticaking agent in feed for all animal species with a maximum level of 20,000 mg/kg complete feed.

3.2. Safety

3.2.1. Absorption, distribution, metabolism and excretion

The FEEDAP Panel considers unlikely that Sepiolitic clay, in common with other clays, will be degraded during their passage through the gastrointestinal tract of target animals or absorbed. Clays are essentially not absorbed, and carry-over to animal tissues/products is therefore not expected.

[15] Technical dossier/ Supplementary information (November 2021)/Annex_V.3.
[16] Technical dossier/ Supplementary information (November 2021)/Annex_VII.
[17] Technical dossier/Section II/Annex_II_8.

However, sepiolite's chemical structure shows the presence of fluorine (F) as $(SiO_2)_nOMgF$ fragments (Santaren et al., 1990), the stability of which could be critical in terms of possible release of fluorine in the gastrointestinal tract and subsequent deposition in edible tissues/products, as a consequence of the use of the additive.

The applicant submitted two studies in support of the stability and low bioavailability of F bound to sepiolite.

Bioavailability and distribution of fluorine in tissues were investigated in rats given sepiolite (Suárez et al., 2008). Three groups of rats were administered by gastric intubation with three different treatments: a solution of 0.45 mg NaF/kg body weight (bw), a solution of 4.5 mg NaF/kg bw or a suspension of sepiolite-feed in water at 1 g sepiolite/kg bw. Samples of plasma, liver, kidney and muscle from six rats (three males and females) were taken at eight different time points during a period of 24 h for measurement of fluorine by potentiometry. Maximum levels of fluorine (3.13 and 0.77 μg/mL for the high and the low level, respectively) in plasma of animals given NaF were reached at 1 h. Fluorine plasma levels of animals given 1 g sepiolite in suspension were 0.12 μg/mL at 1 h. A similar fluorine profile was observed in liver (0.55 μg/g) and in kidney (3.09 μg/g) in the highest dose of NaF group 1 h after administration, elimination being almost complete after 8 h. In the sepiolite group, levels of fluorine in liver and kidney after 1 h from administration were 0.13 and 0.33 μg/g, respectively, and were maintained low over the time. In muscle samples, fluorine levels were similar to the limit of detection (LOD, 0.048 μg/g) in all the samples analysed. This study demonstrated that fluorine present in sepiolite is not absorbed when administered to rats.

The bioavailability of fluorine from sepiolite (maximum fluorine content of 9,800 mg/kg) was studied in laying hens by comparing the absorption of fluorine given in diet as NaF or as sepiolite (Nogareda et al., 1990). Three groups of animals were administered with a control diet (basal diet containing 21 mg F/kg), a diet supplemented with NaF at 217 mg fluorine/kg or a diet containing sepiolite at 2% corresponding to 217 mg fluorine/kg. The experiment started when the animals aged 27 weeks until 64 weeks of age. Fluorine was determined by potentiometry analysis conducted in the tibial bone in five animals from each group at weeks 27, 42 and 63. The same analyses were also conducted on eggshell at weeks 42, 55 and 73. No significant differences were found in the fluorine contents in tibial bone and eggshell in the sepiolite group compared to the control. The content of fluorine in the animals given NaF was four times higher compared to the control ($p < 0.001$).

3.2.1.1. Conclusion on ADME

Sepiolitic clay, in common with other clays, is essentially not absorbed, and carry-over to animal tissues/products is therefore not expected. The FEEDAP Panel considered that fluorine present in the additive remains tightly bound during gastrointestinal passage of target animals. Fluorine absorption, as measured by the leached fluorine, is consistently low and is expected to be excreted in faeces.

3.2.2. Toxicological studies

3.2.2.1. Genotoxicity studies

Bacterial mutation assay

In order to investigate the potential of Sepiolitic clay to induce gene mutations in bacteria, an Ames test was performed according to the Organization for Economic Co-operation and Development (OECD) Test Guideline (TG) 471 and following Good Laboratory Practice (GLP) [redacted]

No increase in the mean number of revertant colonies was observed at any tested condition in any tester strain. Therefore, the Panel concluded that Sepiolitic clay did not induce gene mutations in bacteria under the experimental conditions applied in the study.

In vitro micronucleus test in human lymphocytes

To evaluate the potential of Sepiolitic clay to induce chromosome damage, an *in vitro* micronucleus test was carried out in human lymphocytes according to OECD TG 487 and following GLP. [redacted] No cytotoxicity and no increase of the frequency of micronuclei were observed in binucleated cells after treatment with the test item in any experimental condition. The Panel concluded that Sepiolitic clay did not induce micronuclei in human lymphocytes under the experimental conditions applied in this study.

3.2.2.2. Subchronic toxicity studies

In a non-GLP and non-guideline compliant study,[18] four groups of Wistar rats (5 animals/sex per group) were given feed containing 0 (control), 2, 4 or 6% of Sepiolitic clay for 12 weeks. Body weights were recorded at study initiation, weekly and at study termination. At study termination, a gross necropsy analysis was performed on all animals. Organ weights were recorded for liver and kidneys. All animals were subjected to microscopic examination on skeletal muscle, adipose tissue, liver, kidney and heart. In males, a significant increase of body weight was observed at all tested levels compared to the control group after the third week of study. No differences in body weight were observed among the different Sepiolitic clay levels. In females, a significant increase of body weight compared to the control group was observed in animals given Sepiolitic clay at 2% or 4% but not at 6% after the third week of study. There were no organ weight changes, gross or microscopic lesions attributable to sepiolite administration.

The FEEDAP Panel noted that the study shows a number of significant deviations from the current OECD TG 408. These include a reduced number of animals tested, shorter exposure duration, limited experimental protocol and results reporting. However, owing that the additive is essentially not absorbed, the FEEDAP Panel considered the conclusions of the study acceptable and concluded that Sepiolitic clay given to rats up to 6% in feed for 12 weeks did not induce any adverse effect under the reported experimental conditions.

3.2.2.3. Conclusion on ADME and toxicological studies

The FEEDAP Panel concluded that Sepiolitic clay, as other clays, is essentially not absorbed, and carry-over to animal tissues/products is therefore not expected. Sepiolitic clay is not genotoxic and does not induce any adverse effects following oral administration.

3.2.3. Safety for the target species

In support of the safety of the additive for the target species, the applicant submitted tolerance trials in dairy cows, weaned piglets, chickens for fattening and salmonids.

Dairy cows

[redacted]

[18] Technical dossier/Section III/Annex_III_5.
[19] Technical dossier/Section III/Supplementary Information (November 2011)/Annex_VIII.1.

[redacted] However, these differences were considered not biologically relevant. No other treatment effects were observed neither in the haematological nor in the biochemical parameters.

The FEEDAP Panel concluded that the additive is safe for dairy cows at 20,000 mg/kg feed with a margin of safety of 5.5.

Weaned piglets

In the original dossier, the applicant provided a tolerance study in pigs[22] which was not further considered for the assessment due to major limitations in the study design and reporting (not in compliance with the relevant EFSA guidance, no statistical outputs provided, no raw data analysis available). Another tolerance study was made available to the FEEDAP Panel and is described below.

[redacted][23]

[redacted]

[22] Technical dossier/Section III/Annex_III_6.
[23] Technical dossier/Section III/Supplementary Information (November 2011)/Annex_VIII.2.

[redacted] These differences, however, were not consider biologically relevant.

The FEEDAP Panel concluded that the additive is safe for weaned piglets at 20,000 mg/kg feed with a margin of safety of 2.

Chickens for fattening

[redacted][26]

[redacted]

[26] Technical dossier/Section III/Supplementary Information (November 2011)/Annex_VIII.3.

[redacted]

[redacted]

The supplementation of the experimental diets with Sepiolitic clay at 1× and 2× maximum recommended level had negative effects on the performance of chickens for fattening. The FEEDAP Panel concluded that the additive is safe for chickens for fattening at 10,000 mg/kg feed, which represents 0.5× proposed use level.

Salmonids

[redacted]

[30] Technical dossier/Supplementary Information (November 2021)/Annex VIII.4.

[redacted]

[redacted]

The supplementation of the experimental diets with Sepiolitic clay at 35,200 mg/kg (1.76× maximum recommended level) had negative effects on the performance of juvenile rainbow trout. The FEEDAP Panel concluded that the additive is safe for salmonids at 17,600 mg/kg feed (0.88× the maximum recommended level).

3.2.3.1. Conclusions on safety for the target species

Based on the data from the tolerance trials submitted, the FEEDAP Panel concluded that Sepiolitic clay is safe for dairy cows and weaned piglets at 20,000 mg/kg feed. These conclusions are extrapolated to other dairy ruminants, pigs for fattening and other growing *Suidae*. The additive is safe for chickens for fattening at 10,000 mg/kg feed and for salmonids at 17,600 mg/kg feed.

Considering that it is not possible to establish a comparable margin of safety in the four major species, the Panel cannot conclude on the safety of Sepiolitic clay for other animal species/categories.

It is expected that the additive at the recommended conditions of use will not interfere with the nutrient/micronutrients supply of animals.

3.2.4. Safety for the consumer

The Panel considers that Sepiolitic clay and the other mineral components of the additive are not absorbed, and that it is unlikely that harmful amounts of residues of any chemical component would occur in edible tissues/products as a consequence of the use of Sepiolitic clay in animal nutrition. The use of the additive in animal nutrition is considered safe for the consumers.

3.2.5. Safety for user

3.2.5.1. Effects on the respiratory system

Based on dusting potential data available ([redacted]), the FEEDAP Panel considered that exposure of users to the additive via inhalation is very likely.

No inhalation toxicity study with the additive under assessment has been provided.

The FEEDAP Panel notes that the additive contains crystalline silica ([redacted]). Inhalation of crystalline silica is known to be hazardous and is associated with increased risk of lung cancer and the industrial disease, silicosis. The European Directive 2017/2398 set an occupational exposure limit (OEL) of 0.1 mg/m^3 of air for respirable crystalline silica dust. The applicant submitted data on dusting potential on nine batches made by [redacted] Inhalable, thoracic and respirable fractions were submitted. The relevant respirable fraction was consistently higher for [redacted] method [redacted]. Consequently, [redacted] data will be considered only. The respirable dust fraction of Sepiolitic clay was up to [redacted], corresponding to 16.05 mg crystalline silica/m^3 respirable dust, which is above the OEL.

The highest nickel content analysed in the additive was [redacted]. The highest dusting potential of the product was [redacted], corresponding to about 0.109 mg Ni/m^3 which would exceed the transitional limit value of 0.1 mg Ni/m^3 for the inhalable fraction and 8-hour time-weighted average exposure established in DIRECTIVE (EU) 2022/431[34] and therefore would constitute a hazard for the users by inhalation.

In addition, due to the presence of nickel in the additive, it should be considered as a respiratory sensitiser.

3.2.5.2. Effects on the eyes and skin

The skin irritation potential of Sepiolitic clay was tested in an *in vitro* skin irritation study performed according to OECD TG 439,[35] which showed that the additive is not a skin irritant.

The eye irritation potential of Sepiolitic clay was tested in an *in vitro* study following the principles of GLP and according to OECD TG 437,[36] which showed that the additive is not an eye irritant.

[34] DIRECTIVE (EU) 2022/431 OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL of 9 March 2022 amending Directive 2004/37/EC on the protection of workers from the risks related to exposure to carcinogens or mutagens at work, 16.3.2022, OJ L88 pp.1-14. The limit value of 0.05 mg/m^3 for the inhalable fraction, measured as nickel, shall apply from 18 January 2025. Until then a limit value of 0,1 mg/m^3 shall apply.

[35] Technical dossier/Supplementary Information (November 2021)/Annex X.3.

[36] Technical dossier/Supplementary Information (November 2021)/Annex X.2.

The skin sensitisation potential of Sepiolitic clay was tested in a study following GLP and according to OECD TG 429.[37] The additive did not show any skin sensitisation potential. However, due to the presence of nickel in the additive, it should be considered as a dermal sensitiser.

3.2.5.3. Conclusions on safety for the user

Sepiolitic clay poses a risk by inhalation. It is not irritant to the skin or eyes but should be considered as skin and respiratory sensitiser.

3.2.6. Safety for the environment

Illite and sepiolite are naturally occurring clays widely distributed in the environment. Therefore, it is not expected that the use of the additive in animal nutrition would adversely affect the environment.

3.3. Efficacy

3.3.1. Efficacy of Sepiolitic clay as a binder

To support the efficacy of the additive as a binder, the applicant provided five studies. Three of them had several shortcomings (e.g. lack of parameters relevant to the effect as a binder, lack of statistics and certificate of analysis) and were not further considered in the assessment.

In a study (Angulo et al., 1996), the effect of Sepiolitic clay on pellet durability was studied in two types of chicken for fattening feeds (starter and finisher) and in a feed for pigs. The two diets for chickens for fattening had different fat content (starter 6%, finisher 7.5%), which inversely affect pellet durability, and were manufactured in the form of pellets of 3 mm of diameter. The feed for pigs was manufactured in the form of pellets of two different diameters (3 or 6 mm). Each of the mash feeds (two for chickens and two for pigs (one of each pelleting diameter)) were prepared mixing all the ingredients in a mixer in two separated aliquots to guarantee uniform mixing. One of the two aliquots was mixed with Sepiolitic clay at 0 or 10,000 mg/kg complete feed, the other one with 0 or 20,000 mg/kg complete feed. Pellet durability was measured in four replicates for each feed using the Pfost method. The results were statistically analysed with ANOVA.

The addition of Sepiolitic clay in starter and finisher feeds for chickens for fattening and in feed for pigs (both granulometries) improved the pellet durability, compared to the control (Table 4).

Table 4: Results of pellet durability in feeds supplemented with 0, 10,000 or 20,000 mg Sepiolitic clay/kg

Feed type	Type of feed	Sepiolitic clay inclusion level (mg/kg)	Durability (%)
Chickens for fattening	Starter	0	55.8^{c}
		10,000	60.2^{b}
		0	58.1^{c}
		20,000	64.8^{a}
	Finisher	0	27.7^{b}
		10,000	32.7^{a}
		0	28.9^{b}
		20,000	34.0^{a}
Pigs	3 mm	0	88.4^{b}
		10,000	90.9^{a}
		0	88.0^{b}
		20,000	91.1^{a}
	6 mm	0	83.2^{c}
		10,000	84.7^{b}
		0	81.5^{d}
		20,000	85.6^{a}

^{a,b,c,d}: Mean values within each feed with a different superscript are significantly different ($p < 0.05$).

[37] Technical dossier/Supplementary Information (November 2021)/Annex X.1.

In one study with three *in vitro* trials,[38] [redacted] (Table 5).

Table 5: [redacted]

[redacted]	[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]	[redacted]
	[redacted]	[redacted]	[redacted]
	[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]	[redacted]
	[redacted]	[redacted]	[redacted]
	[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]	[redacted]
	[redacted]	[redacted]	[redacted]
	[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]	[redacted]
	[redacted]	[redacted]	[redacted]
	[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]	[redacted]
	[redacted]	[redacted]	[redacted]
	[redacted]	[redacted]	[redacted]

[redacted]

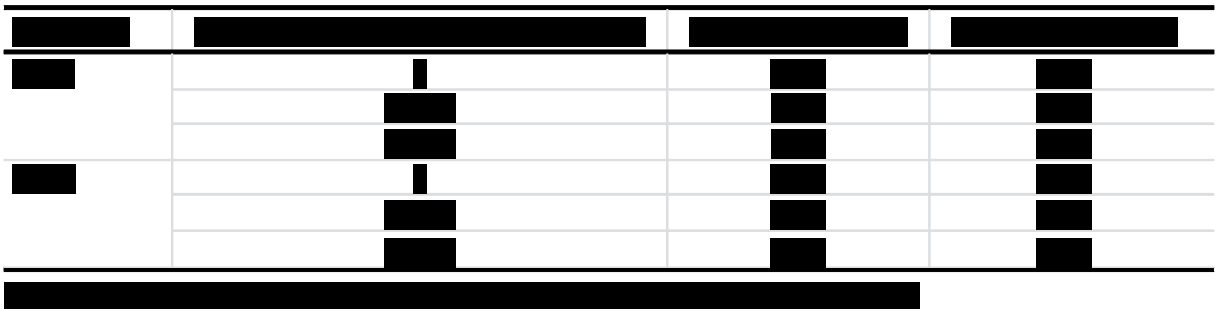
3.3.2. Efficacy of Sepiolitic clay as an anticaking agent

In one study with three *in vitro* trials,[43] [redacted] (Table 6).

Table 6: [redacted]

[redacted]	[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]	[redacted]
	[redacted]	[redacted]	[redacted]
	[redacted]	[redacted]	[redacted]

[38] Technical dossier/Supplementary Information (November 2021)/Annex XII.1.
[39] Chickens for fattening feed main ingredients: maize, soybean meal and animal fat.
[40] Laying hens feed main ingredients: maize, soybean meal and soy oil.
[41] Pig's feed main ingredients: barley, soybean meal and soy oil.
[42] Cow's feed main ingredients maize, soybean meal and wheat.
[43] Technical dossier/Supplementary information (November 2021)/Annex XII.2.



3.3.3. Conclusions on efficacy

Based on the data available covering a wide range of feeds, the FEEDAP Panel concludes that Sepiolitic clay is efficacious as a pellet binder and anticaking agent.

4. Conclusions

The FEEDAP Panel concludes that the additive is safe for dairy cows and for weaned piglets at the recommended use level (20,000 mg/kg feed). The conclusion is extrapolated to other dairy ruminants, pigs for fattening and other growing *Suidae*. The additive is safe for chickens for fattening at 10,000 mg/kg feed and for salmonids at 17,600 mg/kg feed. The Panel cannot conclude on the safety of Sepiolitic clay for other animal species/categories.

The additive, at the proposed conditions of use, is considered safe for the consumers and the environment.

For the user, Sepiolitic clay poses a risk by inhalation. It is not irritant to the skin or eyes but should be considered as skin and respiratory sensitiser.

Based on the data available covering a range of premixtures, feed materials and complete feeds, the FEEDAP Panel concludes that Sepiolitic clay is efficacious as a binder and anticaking agent.

5. Documentation as provided to EFSA/Chronology

Date	Event
28/06/2019	Dossier received by EFSA. Sepiolitic clay as technological additive in feed. Submitted by MYTA S.A
28/06/2019	Reception mandate from the European Commission
09/08/2019	Application validated by EFSA – Start of the scientific assessment
23/10/2019	Request of supplementary information to the applicant in line with Article 8(1)(2) of Regulation (EC) No 1831/2003 – Scientific assessment suspended. *Issues: Characterisation, safety for the target species, safety for the user and efficacy*
23/10/2019	Request of supplementary information to the applicant in line with Article 8(1)(2) of Regulation (EC) No 1831/2003 – Scientific assessment suspended. *Issues: toxicology*
06/11/2019	Reception of the Evaluation report of the European Union Reference Laboratory for Feed Additives
28/09/2021	Comments received from Member States
24/11/2021	Reception of supplementary information from the applicant - Scientific assessment re-started
03/02/2022	Request of supplementary information to the applicant in line with Article 8(1)(2) of Regulation (EC) No 1831/2003 – *Issues: safety for the target species and toxicological studies*
28/02/2022	Reception of supplementary information from the applicant - Scientific assessment re-started
04/05/2022	Opinion adopted by the FEEDAP Panel. End of the Scientific assessment

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Abbreviations

ADFI	average daily feed intake
ADG	average daily gain
AWG	average weight gain
BW	body weight
CAS	chemical abstract service
DMSO	Dimethylsulfoxide
DMI	dry matter intake
EURL	European Union Reference Laboratory
ECM	energy corrected milk
FCR	feed conversion ratio
F:G	feed to gain ratio
GLM	general linear model
GLP	Good Laboratory Practice
HSI	hepatosomatic index

LC-MS/MS	liquid chromatography with tandem mass spectrometry
LOD	limit of detection
LOQ	limit of quantification
NEL	net energy for lactation
OECD	Organization for Economic Co-operation and Development
OEL	occupational exposure limit
PCB	polychlorinated biphenyl
PCBs	polychlorinated biphenyls
PCDDs	polychlorinated dibenzo-paradioxins
PCDFs	polychlorinated dibenzofurans
SCC	somatic cell count
SEM	scanning electron microscopy
SGR	specific growth rate
TEM	transmission Electron Microscopy
TG	test guideline
TMR	total mixed ration
VSI	viscerosomatic index
XRD	X-ray diffraction
XRF	X-ray fluorescence spectroscopy

Annex A – Executive Summary of the Evaluation Report of the European Union Reference Laboratory for Feed Additives on the Method(s) of Analysis of Sepiolitic clay

In the current application, an authorisation is sought under Article 10 for sepiolitic clay under the category/functional group 1(g) and 1(i) 'technological additives'/'binders' and 'anticaking agents', according to the classification system of Annex I of Regulation (EC) No 1831/2003. Specifically, the authorisation is sought for the use of the feed additive for all animal species.

The feed additive (sepiolitic clay) is a product of sedimentary origin, containing a minimum of 40% (w/w) of sepiolite and 25% (w/w) of illite.

The feed additive is intended to be used in premixtures and feedingstuffs. The Applicant suggested a maximum inclusion level of sepiolitic clay of 20 g/kg complete feedingstuffs.

For the determination of the mineralogical composition of the feed additive, the Applicant submitted an X-ray diffraction (XRD) method. Furthermore, the feed additive was characterised by the Applicant using X-ray fluorescence and an atomic absorption spectrometry (AAS).

Based on the experimental evidence provided, the EURL recommends for official control the mineralogical characterisation by X-ray diffraction (XRD) together with the elemental analysis by X-ray fluorescence (XRF) or atomic absorption spectrometry (AAS) for the characterisation of the feed additive.

The Applicant provided no analytical method or experimental data for the determination of sepiolitic clay in premixtures or feedingstuffs, as the unambiguous determination of sepiolitic clay content added to these matrices is not achievable experimentally. Therefore, the EURL cannot evaluate nor recommend any method for official control for the determination of sepiolitic clay in premixtures or feedingstuffs.

Further testing or validation of the methods to be performed through the consortium of National Reference Laboratories as specified by Article 10 (Commission Regulation (EC) No 378/2005, as last amended by Regulation (EU) 2015/1761) is not considered necessary.